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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/551,164	05/31/2006	Shuji Sonezaki	U 015954-0	3215

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LADAS & PARRY LLP
26 WEST 61ST STREET
NEW YORK, NY 10023

EXAMINER	
DO, PENSEE T	

ART UNIT	PAPER NUMBER
1641	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/551,164	SONEZAKI ET AL.	
	Examiner	Art Unit	
	Pensee T. Do	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 August 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/23/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Amendment Entry & Claims Status

The amendment filed on August 8, 2008 has been acknowledged and entered.

Claims 1-17 and newly added 18 are being examined.

Withdrawn Rejection(s)

Rejections under 102 (b) and 103 in the previous office action are withdrawn herein.

New Ground of Rejection

Claim Objections

Claim 9 is objected to because of the following informalities: Claim 9, line 3, recites “a nucleotide” twice. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 10, 11 and 17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 10, 11 and 17 seem to recite a Markush group. If so, please use appropriate Markush language, i.e. selected from the group consisting of A, B and C. Otherwise, please change “and" in last line of the claims to --or--.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the

unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-10, 12 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-13 of copending Application No. 10/551,071 in view of Rohr (US 5,445,970).

Copending application No. 10/551,071 discloses a surface modified titanium dioxide fine particle comprising titanium dioxide having a surface which is modified with a hydrophilic polymer being bonded to hydroxyl group of titanium dioxide via the carboxyl groups on the polymer to form an ester linkage; the titanium is an anatase or rutile form and has a diameter of 2 -200 nm; the polymer is a water-soluble polymer which contains polycarboxylic acid and comprises of a copolymer having a plurality of carboxyl groups; a dispersion liquid of surface modified titanium dioxide fine particles dispersed in an aqueous solvent which the introduction into a living body is acceptable; the aqueous solution is pH buffer solution or a physiological saline.

Copending application '071 differs from the present invention in that it fails to claim the titanium dioxide comprises a molecule having a binding capacity specific for a target molecule being immobilized on the carboxyl groups of the hydrophilic polymer; the molecule having a binding capacity is an amino acid, a peptide, a simple protein, a complex protein or an antibody, nucleotide, nucleic acid, or a peptide nucleic acid, a monosaccharide, a sugar chain, a polysaccharide and a complex carbohydrate.

Rohr teaches magnetic oxide particles coated with a hydrophilic polymer such as methylacrylamide (see col. 12, line 49). The polymer has carboxylic group. The magnetic oxide particle also comprises a specific binder for a target molecule. (see col. 2, lines 63-65). Rohr teaches methylacrylamide polymer (see col. 12, line 49) is hydrophilic and thus water-soluble. Rohr also teaches the polymers are acrylic or methylacrylic acids which are polycarboxylic acids. (see col. 14, line 5). Rohr teaches the specific binder is an amino acid, peptide, simple protein, and complex protein or an antibody, nucleic acid, carbohydrate which are physiological active substances (see col. 5, lines 15-45).

It would have been obvious to one of ordinary skills in the art to incorporate a binder as taught by Rohr to the titanium dioxide surface modified with a hydrophilic polymer as claimed in copending application '071 since both teaches metal particles coated with hydrophilic polymer having carboxyl groups so that the titanium dioxide particle can be used in diagnostic application.

This is a provisional obviousness-type double patenting rejection.

Claim 11 is provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-13 of copending Application No. 10/551,071 in view of Rohr as applied to claim 1 above and further in view of Handy (US 6,997,863).

Copending application '071 and Rohr have been discussed above but fail to teach lipid as a binding agent.

Handy teaches magnetic particles coated with lipid, i.e. liposomes or non-liposomal lipids. Such lipid coating has an advantage of transfecting the magnetic particles into cells or such lipid coating can interact with target ligands for diagnostic application or can be used as a disease marker on cell (see col. 13, lines 55-67, col. 14, lines 18-21).

Thus, it would have been obvious to one of ordinary skill in the art to coat the titanium dioxide particles as claimed by copending application '071 modified with the teaching of Rohr so that magnetic particles can be used in various biological applications, i.e. as a transfecting agent or as a marker on cell or interact with a ligands for use in diagnostic application.

This is a provisional obviousness-type double patenting rejection.

Claims 13-15 and 18 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-13 of copending Application No. 10/551,071 in view of Rohr as applied to claim 1 above and further in view Klaveness et al. (US 5,628,983).

Okabe and Rohr have been discussed above but fail to teach suspending titanium oxide particles in a dispersion liquid such as saline.

Klaveness teaches superparamagnetic particles for use in tumour imaging and detection, wherein the magnetic particles are dispersed in a solution such as saline for administration to a patient. Klaveness teaches that magnetic particles or magnetomeric diagnostic agents are in forms suitable for injection, ingestion or infusion directly or after dispersion in or dilution with physiologically acceptable carrier medium, e.g. water for injection. Thus, the contrast agent must be formulated in conventional administration forms such as powders, solutions, suspensions, dispersions, etc. (see col. 8, lines 46-54). Klaveness further teaches an injectable dispersion comprising dextran coated magnetic particles in saline solution. (see example 1). Klaveness also teaches a freezed- dried dispersion of particles comprising monoclonal antibody coated superparamagnetic particles must be dispersed in saline before administration. (see example 2).

It would have been obvious to one of ordinary skills in the art disperse the titanium oxide particles of Okabe modified by Rohr in a saline buffer as taught by Klaveness because saline aids the administration of the particles to a living body to detect or image tumour cells. Since Okabe teaches that the titanium dioxide particle has advantage as a photocatalyst, and Klaveness teaches that with the saline buffer, the magnetic particles can be injected to a living for imaging or detecting cancer cells, one of ordinary skills in the art can take advantage of the photocalytic property of the titanium dioxide in Okabe and the imaging property of the magnetic particles in saline in

Klaveness to image, detect using magnetic property and destroy cancer cells using photocatalytic property of titanium dioxide.

This is a provisional obviousness-type double patenting rejection.

Claims 16-17 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-13 of copending Application No. 10/551,071 in view of Rohr as applied to claim 1 above and further in view of Kraus, Jr. (US 6,470,220).

Copending application '071 and Rohr have been discussed above but fail to teach magnetic particles encapsulated in liposome.

Kraus teaches magnetic particles encapsulated in liposomes for easy delivery of the magnetic particles as a contrast agent in diagnostic or therapeutic applications (see col. 5, lines 40-42).

It would have been obvious to one of ordinary skills in the art to incorporate the magnetic/titanium oxide of copending application '071 modified by Rohr in a liposome as taught by Kraus so that the use of such magnetic /liposome particles can be expanded into the therapeutic and other diagnostic application such as cancer therapy.

This is a provisional obviousness-type double patenting rejection.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-3, 5-10, 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Okabe (JP 11255516A), please see English translation as a reference.

Okabe teaches a method of producing TiO_2 powder, i.e. crystal, comprising reacting a) a oxypolycarboxylic acid (hydrophilic polymer) with b) a polyol compound and c) a complex alkoxide having a chemical bond of (-Ti-O-Al-O-Ti-) (titanium dioxide and aluminum) to provide water-soluble composite ester complex oligomer (page 1, claim 1). For claim 2, Okabe teaches TiO_2 obtained is anatase, rutile or a mixture of anatase and rutile (see page 22, table 4, [0021]). For claim 5-7, Okabe teaches oxypolycarboxylic acid which is hydrophilic, water-soluble polymer and comprises a plurality of carboxyl groups.

However, Okabe fails to teach that the titanium dioxide particle obtained comprises a binder specific for a target molecule being immobilized on the carboxyl group of the hydrophilic polymer. Such binder is an amino acid, a peptide, a simple protein, a complex protein or an antibody, nucleotide, nucleic acid, or a peptide nucleic acid, a monosaccharide, a sugar chain, a polysaccharide and a complex carbohydrate. Okabe also fails to teach the size range of the particles from 2 nm to 200 nm.

Rohr teaches magnetic oxide particles coated with a hydrophilic polymer such as methylacrylamide (see col. 12, line 49). The polymer has carboxylic group. The magnetic oxide particle also comprises a specific binder for a target molecule. (see col. 2, lines 63-65). Rohr teaches methylacrylamide polymer (see col. 12, line 49) is

hydrophilic and thus water-soluble. Rohr also teaches the polymers are acrylic or methylacrylic acids which are polycarboxylic acids. (see col. 14, line 5). Rohr teaches the specific binder is an amino acid, peptide, simple protein, and complex protein or an antibody, nucleic acid, carbohydrate which are physiological active substances (see col. 5, lines 15-45). Rohr teaches particles size of 0.01 microns (10 nm) to 1000 microns (see col. 12, lines 62-64).

It would have been obvious to one of ordinary skills in the art to incorporate a binder as taught by Rohr to the titanium dioxide surface modified with a hydrophilic polymer as claimed in Okabe since both teach metal particles coated with hydrophilic polymer having carboxyl groups so that the titanium dioxide particle can be used in diagnostic application.

Regarding the size range of the particle, it would have been obvious to one of ordinary skills in the art at the time the invention was made to arrive at the size range of 2 nm to 200 nm, since it has been held that where the general conditions of a claim are disclosed in the prior arts, discovering the optimum or workable ranges involves only routine skills in the art. In re Aller, 105 USPQ 233.

Claim 4 is rejected under 35 U.S.C. 103(a) as being unpatentable over Okabe in view of Rohr as applied to claim 1 above, and further in view of Watson et al. (Journal of Photochemistry and Photobiology A: Chemistry 148 (2002) 303-313). (submitted by Applicants).

Okabe and Rohr have been discussed above but fail to teach incorporating magnetic material into the titanium dioxide particle.

Watson teaches nanocrystalline titanium dioxide particles being coated directly onto a magnetic core. (see abstract). Watson also discloses that modifying the properties of one material by coating it with another type of material has been a popular approach widely documented in the literature. In this work, the concept of coating one material with another is used to develop a novel magnetic photocatalyst. The magnetic core is useful for enhancing the separation properties of suspended particles from solution, whereas the photocatalytic properties of the outer titanium dioxide are used to destroy organic contaminants in wastewaters. (see pg. 301, col. 1, introduction and background, 1st paragraph).

Thus, it would have been obvious to one of ordinary skills in the art to incorporate a magnetic material as taught by Watson with the titanium dioxide particles taught by Okabe modified with Rohr so that the resulted titanium dioxide nanoparticles has an enhanced separation property in solution.

Claim 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over Okabe in view of Rohr as applied to claim1 above, and further in view of Handy (US 6,997,863).

Okabe and Rohr have been discussed above but fail to teach lipid as a binding agent.

Handy teaches magnetic particles coated with lipid, i.e. liposomes or non-liposomal lipids. Such lipid coating has an advantage of transfecting the magnetic particles into cells or such lipid coating can interact with target ligands for diagnostic application or can be used as a disease marker on cell (see col. 13, lines 55-67, col. 14, lines 18-21).

Thus, it would have been obvious to one of ordinary skill in the art to coat the titanium dioxide particles as taught by Okabe modified with the teaching of Rohr so that magnetic particles can be used in various biological applications, i.e. as a transfecting agent or as a marker on cell or interact with a ligands for use in diagnostic application.

Claims 13-15 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Okabe in view of Rohr as applied to claim 1 above, and further in view of Klaveness et al. (US 5,628,983).

Okabe and Rohr have been discussed above but fail to teach suspending titanium oxide particles in a dispersion liquid such as saline.

Klaveness teaches superparamagnetic particles for use in tumor imaging and detection, wherein the magnetic particles are dispersed in a solution such as saline for administration to a patient. Klaveness teaches that magnetic particles or magnetomeric diagnostic agents are in forms suitable for injection, ingestion or infusion directly or after dispersion in or dilution with physiologically acceptable carrier medium, e.g. water for injection. Thus, the contrast agent must be formulated in conventional administration forms such as powders, solutions, suspensions, dispersions, etc. (see col. 8, lines 46-

54). Klaveness further teaches an injectable dispersion comprising dextran coated magnetic particles in saline solution. (see example 1). Klaveness also teaches a freezed- dried dispersion of particles comprising monoclonal antibody coated superparamagnetic particles must be dispersed in saline before administration. (see example 2).

It would have been obvious to one of ordinary skills in the art disperse the titanium oxide particles of Okabe modified by Rohr in a saline buffer as taught by Klaveness because saline aids the administration of the particles to a living body to detect or image tumor cells. Since Okabe teaches that the titanium dioxide particle has advantage as a photocatalyst, and Klaveness teaches that with the saline buffer, the magnetic particles can be injected to a living for imaging or detecting cancer cells, one of ordinary skills in the art can take advantage of the photocalytic property of the titanium dioxide in Okabe and the imaging property of the magnetic particles in saline in Klaveness to image, detect using magnetic property and destroy cancer cells using photocatalytic property of titanium dioxide.

Claims 16-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Okabe in view of Rohr as applied to claim1 above, and further in view of Kraus, Jr. (US 6,470,220).

Okabe and Rohr have been discussed above but fail to teach magnetic particles encapsulated in liposome.

Kraus teaches magnetic particles encapsulated in liposomes for easy delivery of the magnetic particles as a contrast agent in diagnostic or therapeutic applications (see col. 5, lines 40-42).

It would have been obvious to one of ordinary skills in the art to incorporate the magnetic/titanium oxide of Okabe modified by Rohr in a liposome as taught by Kraus so that the use of such magnetic /liposome particles can be expanded into the therapeutic and other diagnostic application such as cancer therapy.

Response to Arguments

Applicant's arguments with respect to claims 1-17 have been considered but are moot in view of the new ground(s) of rejection.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Pensee T. Do whose telephone number is 571-272-0819. The examiner can normally be reached on Monday-Friday, 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark Shibuya can be reached on 571-272-0806. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Christopher L. Chin/
Primary Examiner, Art Unit 1641

/Pensee T. Do/
Examiner, Art Unit 1641